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EXAMINER	
STAPLES, MARK	
ART UNIT	**PAPER NUMBER**
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/510,034	PAN, SHEN QUAN	
	Examiner	Art Unit	
	Mark Staples	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/01/2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *21-24,26, and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20 and 25* is/are rejected.

7)☒ Claim(s) *7,12,14-16 and 20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 October 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/01/2004 & 02/10/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of claims 1-20 of Group 1 in the reply filed on 12/01/2006 is acknowledged. The traversal is on two grounds that: (1) there is a unifying technical feature for the claim set of "transformation" or "transfection" and (2) the kit of claim 15 should be examined with processes of Group I.

The first argument is not found persuasive because according to PCT Rule 13.1 there must be the same or a corresponding special technical feature as to form a single general inventive concept. Neither "transformation" nor "transfection" is a *special* technical feature. "Transformation" and "transfection" are technical features which are well known in the prior art (for instance, see Patil et al., cited on the Information Disclosure Statement, IDS, on p. 129, col. 2, line 1 and last sentence of the legend to Figure 2). Furthermore, the different processes of the restriction Groups I-IV are not conclusory as Applicant's Representative states, but are evidentiary, as these are the different processes recited in the claims.

The Lack of Unity requirement is still deemed proper and is therefore made FINAL.

The second argument is found persuasive enough for inclusion of the kit of claim 25 in the main invention of Group I, per PCT Article 17(3)(a) and 37 CFR § 1.476(c).

In summary, claims 1-20 of Group 1 and claim 25 as filed 10/10/2004 will be fully examined for patentability.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The title should be clarified, the use the term "(void)" is unclear, the construction of the phrase "of introduced dna . . . in transit" is unclear, and "dna" should be capitalized.

4. The use of the trademark PICOGREEN® has been noted in this application. It and any other trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

5. Claim 7 is objected to because of the following informalities: the singular "step" in line 2 should be changed to the plural "steps", as several steps are recited in this claim. Appropriate correction is required.

6. Claim 12 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. It is noted that the preamble of this claim recites certain elements not found in antecedent claim 1 but these preamble elements are not recited as active methods steps and do not carry patentable weight.

7. Claim 14 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. It is noted that the preamble of this claim recites certain elements not found in antecedent claim 1 but these preamble elements are not recited as active methods steps and do not carry patentable weight.

8. Claims 15 and 16 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claims 15 and 16 have not been further treated on the merits.

9. Claim 20 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 20, dependent on claim 1, recites a step of permeabilizing the cell before contacting the cell with a probe but this is a duplication of claim 1 as the cells are already "permeabilized cells" when they are contacting the probe. Any amendment of the claims 1 and 8 should avoid claiming the same process twice. See also the rejection below for claim 1 concerning omitting an essential step.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 recites the limitation "permeabilized" in line 6. There is insufficient antecedent basis for this limitation in the claim.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: permeabilizing the cell.

The term "risk" in claim 7 is a relative term which renders the claim indefinite. The term "risk" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unknown and hence unclear what is considered a risk. The specification only provides examples of risk associated with the process and does not define the term of "risk'. What may be a risk depends on what the process is used for. Cell death may be a risk, in a process that seeks to continue a cell line, such as incorporation of a gene for expressing that gene, but may be benefit in another process which seeks to destroy cells, such as incorporating a nucleic acid into cancerous cells in order to destroy them.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Due to the claim rejections given above, the claims are interpreted as follows for determining the applicability of prior art.

12. Claims 1-4, 7, 8, 10, 12-14, 17, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Ainger et al. (1993) cited on the Information Disclosure Statement, IDS.

Regarding claims 1 and 20, Ainger et al. (1993) teach a process for monitoring exogenous nucleic acid in transit, the nucleic acid having been introduced into a cell, the process comprising:

(a) providing a biological sample containing cells into which exogenous nucleic acid has been introduced, wherein the exogenous nucleic acid is in transit (see Title: "Transport and Localization of Exogenous Myelin Basic Protein mRNA Microinjected into Oligodendrocytes");

(b) fixing the cells; and

(c) subjecting the cells to an in situ hybridization procedure which comprises contacting the permeabilized cells with a probe which hybridizes to the exogenous nucleic acid (for these steps, 1(b) and 1(c) see p. 433, the first three sentences in the section *In situ Hybridization*: "In situ hybridization was performed according to the protocol of Singer etal. (1986) with minor modifications. The procedure was carried out shortly after fixation of the cells with paraformaldehyde as described above" with a "Digoxigenin-labeled probe"; see on the same page, the 1st sentence of the 3rd paragraph: "Labeling for tubulin was performed on fixed cells after permeabilization with detergent"); and

(d) visualizing the exogenous nucleic acid in transit (see last sentence of p. 433 continued to p. 444: "Time lapse confocal image collection was controlled by a

specialized command file written for this purpose" and for further clarification see the laste sentence of the Abstract : "This work represents the first characterization of intracellular movement of mRNA [transit] in living cells . . .").

Regarding claim 2, Ainger et al. (1993) teach a process for determining the number of exogenous nucleic acid in the cytoplasm (for determination of the number, amount, of exogenous nucleic acid see p. 439, 2nd col., 1st sentence: "However, the number of exogenous RNA granules in the microinjected cells (which reflects the amount of exogenous MBP mRNA) was generally greater than the number of endogenous RNA granules observed by in situ hybridization (which reflects the amount of endogenous MBP mRNA)" and that the nucleic acid is in the cytoplasm see p. 434, 2nd sentence under the section *Microinjected MBP mRNA Forms IntraceUular Granules*: "The injected RNA appeared as small granules which were present throughout the cytoplasm").

Regarding claim 3, Ainger et al. (1993) teach a process for determining whether the exogenous nucleic acid is in the cytoplasm (see p. 434, 2nd sentence under the section *Microinjected MBP mRNA Forms IntraceUular Granules*: "The injected RNA appeared as small granules which were present throughout the cytoplasm").

Regarding claim 4, Ainger et al. (1993) teach a process for determining the length of time required for the exogenous nucleic acid to appear in the cytoplasm (see p. 435, 3rd sentence under the section *Time Lapse Analysis of MBP mRNA Granule Formation in Oligodendrocytes*: "To analyze the dynamics of RNA granule formation,

fluorescein-labeled MBP mRNA was microinjected into oligodendrocytes, and series of sequential images were collected at different time points" and see p. 435 last sentence: "These results indicate that MBP mRNA forms granules soon after it appears in the cytoplasm and that the granules are rapidly transported to the periphery of the cell").

Regarding claim 7, Ainger et al. (1993) teach a process for assessing risk associated with introduction of the exogenous nucleic acid into the cell, the process further comprising the step of

determining the number of exogenous nucleic acid in the cytoplasm and in the nucleus at different time intervals after the exogenous nucleic acid has been introduced;

determining the ratio of exogenous nucleic acid in the nucleus to cytoplasm at each interval; and

predicting, in accordance with said ratio and number of exogenous nucleic acid introduced, the risk associated with introduction of the exogenous nucleic acid into the cell (see p. 435, the section *Time Lapse Analysis of MBP mRNA Granule Formation in Oligodendrocytes* where both the nucleus and cytoplasm are monitored with time and only granules appear in the cytoplasm with the risk being: T"hese results indicate that MBP mRNA forms granules soon after it appears in the cytoplasm and that the granules are rapidly transported to the periphery of the cell").

Regarding claim 8, Ainger et al. (1993) teach a process for determining the optimum parameters for obtaining a desired copy number of exogenous nucleic acid introduced into the cell, the process comprising:

(a) introducing an exogenous nucleic acid into a cell under a set of parameters (see section *Microinjection and Immunocytochemistry* on p. 433 for parameters including temperature, concentration, and time);

(b) monitoring the exogenous nucleic acid according to the process defined in claim 1 to determine the number of exogenous nucleic acid in the cytoplasm or in the nucleus at different time intervals after the nucleic acid has been introduced (see regarding claim 1 above); and

(c) determining the set of parameters under which the exogenous nucleic acid is delivered in the desired copy number into the cell.

Regarding claim 8, Ainger et al. (1993) teach a process wherein one of the parameters is the length of time in which the exogenous nucleic acid is in contact with the cell (see p. 433, 3rd sentence of 2dn paragraph: "Cells injected with digoxiganin-RNA were incubated at 37°C, for 10 rain, to allow time for RNA transport").

Regarding claim 10, Ainger et al. (1993) teach a process where one of the parameters is the ability of a gene delivery vector to deliver the exogenous nucleic acid (see p. 432, 2nd col., 2nd sentence of 2nd paragraph for "SP6 [gene] vector").

Regarding claim 12, Ainger et al. (1993) teach a process for identifying whether a cell contains an exogenous nucleic acid, wherein the exogenous nucleic acid is free of sequences encoding a selection marker or reporter protein intended to select for or identify the cell as containing the exogenous nucleic acid, the process comprising:

(a) introducing the exogenous nucleic acid into the cell (see Title: "Transport and Localization of Exogenous Myelin Basic Protein mRNA Microinjected into Oligodendrocytes"); and

(b) monitoring the exogenous nucleic acid according to the process defined in claim 1; wherein visualization of the nucleic acid in the cell indicates that the cell contains the exogenous nucleic acid (see last sentence of p. 433 continued to p. 444: "Time lapse confocal image collection was controlled by a specialized command file written for this purpose" and for further clarification see the last sentence of the Abstract : "This work represents the first characterizationof intracellular movement of mRNA [transit] in living cells . . .").

Regarding claim 13, Ainger et al. (1993) teach a process for identifying a molecular marker associated with the competency of a cell to receive exogenous nucleic acid, wherein the cell comprises an antigen, the process comprising:

(a) introducing an exogenous nucleic acid to the cell (see Title: "Transport and Localization of Exogenous Myelin Basic Protein mRNA Microinjected into Oligodendrocytes");

(b) monitoring the exogenous nucleic acid according to the process defined in claim 1 (see regarding claim 1, above);

(c) testing the fixed cells for binding of the antigen with an antibody, wherein the antibody is capable of binding to the antigen in the fixed and permeabilized cell (see section *Microinjection and Immunocytochemistry* on p. 433 where the antibody Alkaline

phosphatase-conjugated polyclonal Fab anti-digoxigenin binds to the antigen -RNA after cell fixation); and

(d) determining whether the antigen co-localizes with the exogenous nucleic acid in transit; wherein co-localization of the exogenous nucleic acid in transit with the antigen indicates that the antigen is a molecular marker associated with transformation competency (see Figure 1 for co-localization of the method by Ainger et al. which occurs because the antigen, digoxiganin, is covalently linked to the nucleic acid, RNA).

Regarding claim 14, Ainger et al. (1993) teach a process for identifying a cell that is competent for receiving exogenous nucleic acid, the process comprising monitoring the exogenous nucleic acid according to the process defined in claim 1 for presence of the exogenous nucleic acid in the cell (see regarding claim 1 above).

Regarding claim 17, Ainger et al. (1993) teach a process wherein the in situ hybridization procedure is fluorescence (see p. 433, 6th sentence in the section *In situ Hybridization*: ". . . in situ hybridization Immunocytochemistry was performed using a mouse mAb to digoxigenin . . . and fluorescein- or Texas red-conjugated goat anti-mouse antibodies").

13. Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Patil et al. (1996) cited on the Information Disclosure Statement, IDS.

Regarding claim 1, Patil et al. teach a process for monitoring exogenous nucleic acid in transit, the nucleic acid having been introduced into a cell, the process comprising:

(a) providing a biological sample containing cells into which exogenous nucleic acid has been introduced, wherein the exogenous nucleic acid is in transit (see 1st sentecen of Abstract: "Mature sperm cells of zebrafish (*Danio rerio*) incubated with foreign DNA have the capacity to take up foreign DNA. Such uptake can be enhanced by electroporation");

(b) fixing the cells (see last sentence of p. 122: "A portion of the sperm treated with radiolabeled or non-labeled plasmid DNA were fixed . . . "); and

(c) subjecting the cells to an in situ hybridization procedure which comprises contacting the permeabilized cells with a probe which hybridizes to the exogenous nucleic acid and

(d) visualizing the exogenous nucleic acid in transit (for these steps, 1(c) and 1(d) see p. 122, 2nd sentence under the section *Experimental Design*: "For the latter, light microscopic autoradiography and ultrastructural in situ hybridization (UISH) methods were used" and see p.128, 1st sentence: The permeability of the mammalian sperm nucleus to foreign DNA would in essence ensure the chances of its being carried to the fertilized ova . . .").

Regarding claim 3, Patil et al. teach a process for determining whether the exogenous nucleic acid is in the nucleus (see last two sentences of the Abstract: "Ultrastructural in situ hybridization on thin sections of zebrafish spermatozoa, however, was able to show that the exogenous DNA was internalized into the nucleus and that electroporation enhanced this internalization. The results provide direct evidence for

nuclear internalization of foreign DNA by non-mammalian sperm as in mammalian sperm").

14. Claims 1, 11, 18, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al. (1998) cited on the IDS.

Regarding claim 1, Chen et al. teach a process for monitoring exogenous nucleic acid in transit, the nucleic acid having been introduced into a cell, the process comprising:

(a) providing a biological sample containing cells into which exogenous nucleic acid has been introduced, wherein the exogenous nucleic acid is in transit (see Title: "Cointegration of DNA Molecules Introduced into Mammalian Cells by Electroporation" and 2nd sentence of the Abstract for exogenous nucleic acid, that is an E. coli: ". . . gene E. coli gene for guanine phosphoribosyltransferase (gpt) were co-electroporated and gpt + transfectants selected");

(b) fixing the cells (see p. 250, 2nd sentence of the section *Fluorescence In Situ Hybridization*: "Mitotic cells were fixed in methanol-acetic acid . . .");

(c) subjecting the cells to an in situ hybridization procedure which comprises contacting the permeabilized cells with a probe which hybridizes to the exogenous nucleic acid (see p. 250-251, for the section *Fluorescence In Situ Hybridization* and 1st sentence on p. 250: "cells that became permeabilized . . "); and

(d) visualizing the exogenous nucleic acid in transit (see Figures 1 and 3, and especially for Figure 2 where the metaphase and interphase show the transfection, that is the transit, of *dhr* and *gpt* genes).

Regarding claim 11, Chen et al. teach a process for determining the proportion of cells competent to receive exogenous nucleic acid, the process comprising:
(a) introducing an exogenous nucleic acid to a portion of a population of cells;
(b) monitoring the exogenous nucleic acid according to the process defined in claim 1 to determine the presence of the exogenous nucleic acid in the cell (see regarding claim 1 above); and
(c) determining the number of cells in which the exogenous nucleic acid is present as a proportion of the portion of cells, wherein the proportion is the proportion of cells of the population competent to receive the exogenous nucleic acid (see p. 250, 1st sentence: "Here cotransfection could be explained if there were only a minority population [a low number of cells] of competent cells produced (i.e., cells that became permeabilized) . . .")

Regarding claims 18 and 19, Chen et al. teach a process wherein the cell is a plant cell (see p. 254, 3rd sentence under the section *Discussion*).

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Ainger et al. (1993), Ainger et al. (1997), Patil et al. (1996), or Chen et al. (1998) as applied to claim 1 above, and further in view of Dean (2000).

Ainger et al. (1993), Ainger et al. (1997), Patil et al. (1996), and Chen et al. (1998) teach as noted above.

Ainger et al. (1993), Ainger et al. (1997), Patil et al. (1996), and Chen et al. (1998) do not specifically teach a process a process for determining the length of time required for the exogenous nucleic acid to appear from the cytoplasm to the nucleus by measuring the exogeneous nucleic acid in the nucleus and in the cytoplasm

Regarding claims 5 and 6, Dean teaches a process for determining the length of time required for the exogenous nucleic acid to appear from the cytoplasm to the nucleus by measuring the exogeneous nucleic acid in the nucleus and in the cytoplasm (see entire article but especially p. 89, 1st paragraph : "They [Felgner and colleagues] were able to demonstrate that liposomes efficiently delivered fluorescently- labeled PNA-complexed plasmids to the cells, and that the plasmids localized to vesicles within the cytoplasm at early times after transfection (3 h). Interestingly, no nuclear localization of fluorescent plasmid was observed until after cell division, whereas the majority of fluorescently- advantage of the polyamide PNA/ oligonucleotide complexes delivered into the cells by liposomes localized to the nucleus within 3 h" and Dean goes on to

teach other methods of monitoring plasmid transport in the cytoplasm and the nucleus with time).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the processes of Ainger et al. (1993), Ainger et al. (1997), Patil et al. (1996), or Chen et al. (1998) monitoring exogenous nucleic acid time course of transit in the cytoplasm and nucleus as suggested by Dean with a reasonable expectation of success. The motivation to do so is provided by Dean who teaches: "In order for these areas [specific targeting, levels and duration of gene expression] to be optimized, efficient tools for real-time study of plasmids in cell systems are required" including the movement of plasmids within cells (see p. 88, 2nd last and last sentence continued to p. 89). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

17. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ainger et al. (1993) in view of Zavada et al. (US Patent No. 6,204,370 issued Mar. 20, 2001).

Ainger et al. (1993) teach reagents for fixing cells (see p. 443, 1st paragraph), a reagent for permeabilizing cells which is a detergent (see p. 443, 3rd paragraph, 1st sentence), and reagents for in situ hybridization (see p. 443, 2nd paragraph).

Ainger et al. (1993) do not teach a kit.

Zavada et al. teach a kit comprising a labeled probe for the visualization of the hybridized probe (see claims 20, 44, and 57).

It is noted that the kit instructions and kit process in claim 25 of the instant application carry no patentable weight, as the kit components can be used for processes which are not recited in the instructions and which are not the recited process.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the components taught by Ainger et al. (1993) into a kit as suggested by Zavada et al. with a reasonable expectation of success. The motivation to do so is provided by Zavada et al. who teach "Test kits of this invention can comprise the nucleic acid probes of the invention which are useful diagnostically/prognostically for neoplastic and/or pre-neoplastic disease" (see col. 3, lines 26-32). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

18. No claim is free of the prior art.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 7:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples MS
Examiner
Art Unit 1637
December 8, 2006

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